Test Material: Pymetrozine

MRID: 49921305

Title: Pymetrozine. Metabolism of [6-^{14}C] Triazine CGA215944 Under Aerobic Conditions in Aquatic Systems. Final Report.

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For CDM/CSS-Dynamac JV

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Date: 11/2/16

This Data Evaluation Record may have been altered by the Environmental Fate and Effects Division subsequent to signing by CDM/CSS-Dynamac JV personnel.

Aerobic degradation of Pymetrozine in aquatic systems

Report:	MRID 49921305. Schulze-Aurich, J. 1996. Pymetrozine. Metabolism of [6-^{14}C] Triazine CGA215944 Under Aerobic Conditions in Aquatic Systems. Final Report. Unpublished study performed by Ciba-Geigy Ltd., Basel, Switzerland; sponsored by Syngenta Ltd, Berkshire, UK; and submitted by Syngenta Crop Protection, LLC, Greensboro, North Carolina. Report No.: 93SA03. Task No.: TK0261457. Experiment started December 6, 1993, and completed February 14, 1995 (p. 8). Final Report issued January 10, 1996.
Document No.:	MRID 49921305
Guideline:	OPPTS 835.4300
Statements:	The study was conducted in accordance with OECD and Swiss GLP standards (pp. 3, 5). Signed and dated Data Confidentiality, GLP, and Quality Assurance statements were provided (pp. 2-3, 5-6). A certification of the authenticity of the report was not included; a certification of the authenticity of Appendix 1: Spectroscopy Report was provided (p. 82). An audit of the final report is listed in the Quality Assurance statement (p. 6).
Classification:	This study is classified SUPPLEMENTAL. Limits of Detection (LOD) and Quantification (LOQ) were not reported. Length and conditions of storage of the water and sediment extract were not reported.
PC Code:	101103
Reviewer:	Jessica Joyce, MS, Fate Scientist U.S. EPA Signature: Date: 2017.07.19 11:28:13 -04'00' Date: July 19, 2017
Secondary Reviewer:	Rochelle F. H. Bohaty, PhD, Senior Chemist U.S. EPA Signature: Rochelle F H Bohaty Date: July 19, 2017

Executive Summary

The aerobic transformation of [triazinyl-6-^{14}C]pymetrozine (CGA 215944) was studied in pond water:silt loam sediment systems (system pH 6.80; sediment organic carbon 3.70%) and Rhine River water:silt loam sediment systems (system pH 7.10; sediment organic carbon 3.20%) from Switzerland that were treated 0.1349 mg/sample (*ca*. 0.27 mg/L, equivalent to a field rate of 0.9 kg a.i./ha or 0.8 lb a.i./A) and incubated in the dark at 20°C for 361 days. Single samples (one entire flask) of each test system was collected at each sampling interval. In the water columns of the pond systems following treatment, redox potentials and oxygen saturation were +151 to +307 mV and 6.0-7.1 mg/L, respectively, with redox potentials in the sediment of -92 to -34 mV and pHs of the test system of 8.43-8.72. In the water columns of the river systems, redox potentials and oxygen saturation were +174 to +313 mV and 6.1-7.3 mg/L, respectively, with redox potentials in the sediment of -81 to -30 mV and pHs of the test systems of 8.44-8.67. In both test systems, the water was oxic and the sediment suboxic throughout the experiment. The test system was viable throughout the experiment.

In pond water:silt loam sediment systems, overall recoveries averaged 105.94 ± 2.94% (sample range 100.16-109.51%) of the applied. Recoveries were within guideline criteria (90-110%). In the water column, pymetrozine decreased from a maximum of 98.10% at time 0 to 0.24-0.33% at 280-361 days posttreatment. Pymetrozine concentrations in the sediment extracts were not reported.

In river water:silt loam sediment systems, overall recoveries averaged 105.67 ± 3.00% (sample range 100.07-108.59%) of the applied. Recoveries were within guideline criteria (90-110%). In the water column, pymetrozine decreased from a maximum of 96.74% at time 0 to 0.36% at 361 days posttreatment. Pymetrozine concentrations in the sediment extracts were not reported.

In the water from the pond water:sediment systems, radioactive residues decreased from 99.39% of the applied at time 0 to 3.98% at 361 days posttreatment. In the sediment, ambient extractable radioactivity increased from 0.55% at time 0 to a maximum of 57.25% at 28 days and was 32.74% at 361 days. Soxhelt extraction released up to an additional 3.41%. Unextracted radioactivity increased from 0.23% at time 0 to a maximum of 46.88% at 203 days and was 43.31% at 361 days. Harsh extraction of the sediment at 203 days released an additional 2.06%. CO_2 was a maximum of 24.66% at 361 days. Organic volatile compounds were not detected at any sampling interval.

In the water from the river water:sediment test systems, radioactive residues decreased from 98.82% of the applied at time 0 to 6.74-7.10% at 280-361 days posttreatment. In the sediment, ambient extractable radioactivity increased from 1.04% at time 0 to a maximum of 62.55% at 28 days and was 31.49% at 361 days. Soxhelt extraction released up to an additional 4.67%. Unextracted radioactivity increased from 0.21% at time 0 to a maximum of 43.27% at 361 days. Harsh extraction of the sediments at 203 days released an additional 2.06%. CO_2 was a maximum of 22.89% at 361 days. Organic volatile compounds were not detected at any sampling interval.

Observed DT_{50} values, calculated half-lives, and information on transformation products are listed in **Table 1**. Pymetrozine dissipated with a DFOP Slow $t_{1/2}$ value of 321 days in the pond water:sediment system and 379 days in the river water:sediment system. Three transformation products were identified.

Table 1. Results Synopsis: Aerobic Aquatic Metabolism of Pymetrozine in the Total System.[1]

Total System	Observed DT_{50} (days)	Calculated Half-life (days)[1]	Model Parameters and Statistics[1]	Transformation Products Common Name (maximum % AR, associated interval)[2]	
				Major	Minor
Switzerland Pond water:silt loam sediment, (20°C, water pH not reported, sediment pH 6.80)	28-60	Slow $t_{1/2}$ = 321 DFOP	C_0 = 99.2 f = 0.514 k_0 = 0.057 k_1 = 0.00216 S_C = 153 S_{SFO} = 1.08e+03	Metabolite D (17.72%, 14 days; $t_{R\ IORE}$ = 109 days) Unextracted residues (46.88%, 203 days) CO_2 (24.66%, 361 days)	Metabolite B (3.70%, 203 days) Metabolite C (2.45%, 361 days)
Switzerland Rhine River water:silt loam sediment, (20°C, water pH not reported, sediment pH 7.10)	60-120	Slow $t_{1/2}$ = 379 DFOP	C_0 = 97.8 f = 0.465 k_0 = 0.0255 k_1 = 0.00183 S_C = 92.4 S_{SFO} = 500	Metabolite D (12.44%, 28 days; SFO DT50 = 121 days) Unextracted residues (43.27%, 361 days) CO_2 (22.89%, 361 days)	Metabolite B (5.87%, 203 days) Metabolite C (4.59%, 361 days)

1 Calculated half-lives and model parameters in accordance with NAFTA kinetics guidance (USEPA, 2012); Double First Order in Parallel (DFOP), Indeterminate Order Rate Equation (IORE), Single First Order (SFO).

2 AR means “applied radioactivity”.

Metabolite B = CGA 294849; 4-Amino-6-methyl-1,2,4-triazine-3,5(2H,4H)-dione.

Metabolite C = CGA 3710754; 4,6-Dimethyl-2H-1,2,4-triazine-3,5-dione.

Metabolite D = CGA 359009; 4,5-Dihydro-5-hydroxy-6-methyl-4-[(3-pyridinylmethylene)amino]-1,2,4-triazine-3-(2H)-one.

Page numbers cited in this DER refer to the numbers in the lower right hand corner of each page.

I. Materials And Methods

A. Materials:

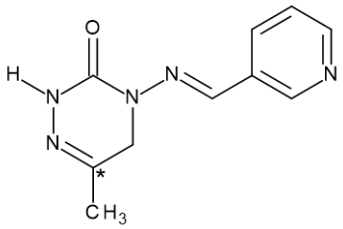
1. Test Material: [Triazinyl-6-^{14}C]pymetrozine (p. 21)

Specific activity: 2.02 MBq/mg

Radiochemical purity: 96.6%

Chemical purity: Not reported

Batch No.: CFQ 6755



Solubility in water: 270 mg/L at 20°C (p. 19)

2. Reference Compounds: The following compounds were used in the analysis.

Table 2. Reference Compounds.

Applicant's Code Name	Chemical Name	Purity (%)	Batch No.
Pymetrozine (CGA 215944)	(E)-4,5-Dihydro-6-methyl-4-(3-pyridylmethyleneamino)-1,2,4-triazin-3(2H)-one	>99.7	AMS 522/102
CGA 359009 (Metabolite D)	4,5-Dihydro-5-hydroxy-6-methyl-4-[(3-pyridinylmethylene)amino]-1,2,4-triazine-3-(2H)-one	--	Project 001AM02
CGA 215525	4-Amino-6-methyl-2,5-dihydro-1,2,4-triazin-3-one	100	HK-6613 U
CGA 249257	6-Methyl-4,5-dihydro-2H-1,2,4-triazin-3-one	98	V-8508/R
CGA 294849 (Metabolite B)	4-Amino-6-methyl-1,2,4-triazine-3,5(2H,4H)-dione	99	HK-8509/R
CGA 311892	4-Amino-6-(hydroxymethyl)-2,5-dihydro-1,2,4-triazin-3-one	99	V-8897/3R
CGA 245342	6-Methyl-4-[(E)-(1-oxidopyridin-1-ium-3-yl)methyleneamino]-2,5-dihydro-1,2,4-triazin-3-one	89.9	OK-7926
CGA 259168	N-(6-Methyl-3-oxo-2,5-dihydro-1,2,4-triazin-4-yl)acetamide	99	HK-8508/2A
CGA 313124	6-(Hydroxymethyl)-4-[(E)-3-pyridylmethyleneamino]-2,5-dihydro-1,2,4-triazin-3-one	99	HK-8903/3R
CGA 320481	4-Amino-2,5-dihydro-1,2,4-triazin-3-one	96 ± 2	HK-9067/2R
CGA 320484	4-[(E)-3-Pyridylmethyleneamino]-2,5-dihydro-1,2,4-triazin-3-one	97	HK-9071/2.R
CGA 323584	6-Methyl-4-[(E)-3-pyridylmethyleneamino]-2H-1,2,4-triazine-3,5-dione	93 ± 2	RV-2437/2
GS 23199	6-Methyl-2H-1,2,4-triazine-3,5-dione	99	A 1507

Data obtained from pp. 18-19, 38-39, and Table 1, pp. 42-43, of the study report, and DER Attachment 1.
-- = not reported.

3. Water:Sediment: Water and sediment collection and characterization are summarized in **Table 3** and **Table 4a-4b**, respectively.

Table 3. Water:Sediment Collection and Storage.

Description		Pond	River
Geographic location		Fröschweiher/Rheinfelden AG/Switzerland	Möhlin/AG/Switzerland
Site description		Pond	Rhine River
Pesticide use history at the collection site		Not reported	
Collection date		November 4, 1993	October 4, 1993
Collection procedures	Water:	Not reported	
	Sediment:		
Storage conditions	Water:	Not reported	
	Sediment:		
Storage length		Water and sediment were stored together while the water was aerated; 4 days for pond, 15 days for river.	
Preparation	Water:	Not reported	
	Sediment:	Sieved (2-mm)	

Data obtained from p. 22 and Table 2, p. 44, in the study report.

Table 4a. Parameters for Characterization of Water:Sediment Samples – Pond.

Parameter (unit)		Field Sampling/ Post Handling	Stage of Test Procedure		
			0 days	203 days	361 days
Water					
Temperature (ºC)		--			
pH		--	--	--	--
Hardness (°d)		17.6			
TOC (mg/L)		8.5	--		--
O_2 Content (mg/L)		--	6.5	6.6	6.8
Redox potential (mV)			+256	+250	+217
Sediment					
Sampling Depth		--			
pH[1]		6.80	8.72	8.67	8.58
Soil Texture		Silt loam			
Particle Size Distribution (%)	Sand	24.70			
	Sandy	50.50			
	Clay	24.8			
Organic matter (%)[2]		6.4			
Organic carbon (%)		3.70			
CEC (mMol/Z/100 g)		25.60			
Microbial biomass (mg C/100 g)[3]		--	422	364	281
Redox potential (mV)			-68	-48	-53

Data obtained from p. 35 and Tables 2-4, pp. 44-46, in the study report. Although it appears likely that the particle size ranges were not equivalent to the USDA system, the USDA sediment texture was approximated by the reviewer using USDA-NRCS technical support tools.

1 Post handling pH determined in KCl (Table 2, p. 44). pH during the experiments was only reported for the total system (Table 4, p. 46)

2 Organic matter determined by the reviewer as: organic matter (%) = organic carbon (%) x 1.72.

3 Microbial biomass is for 118 days rather than 203 days (p. 35).

-- = not reported

Table 4b. Parameters for Characterization of Water:Sediment Samples – River.

Parameter (unit)		Field Sampling/ Post Handling	Stage of Test Procedure		
			0 days	203 days	361 days
Water					
Temperature (ºC)		--			
pH		--	--	--	--
Hardness (°d)		17.0			
TOC (mg/L)		4.7	--		--
O_2 Content (mg/L)		--	6.6	6.1	7.3
Redox potential (mV)			+313	+241	+215
Sediment					
Sampling Depth		--			
pH[1]		7.10	8.66	8.64	8.63
Soil Texture		Silt loam			
Particle Size Distribution (%)	Sand	8.60			
	Sandy	67.20			
	Clay	24.2			
Organic matter (%)[2]		5.50			
Organic carbon (%)		3.20			
CEC (mMol/Z/100 g)		21.60			
Microbial biomass (mg C/100 g)[3]		--	243	135	118
Redox potential (mV)			-65	-55	-30

Data obtained from p. 35 and Tables 2-4, pp. 44-46, in the study report. Although it appears likely that the particle size ranges were not equivalent to the USDA system, the USDA sediment texture was approximated by the reviewer using USDA-NRCS technical support tools.
1 Post handling pH determined in KCl (Table 2, p. 44). pH during the experiments was only reported for the total system (Table 4, p. 46)
2 Organic matter determined by the reviewer as: organic matter (%) = organic carbon (%) x 1.72.
3 Microbial biomass is for 120 days rather than 203 days (p. 35).
-- = not reported

B. Study Design

1. Experimental Conditions: Table 5 summarizes the experimental conditions.

Table 5. Experimental Design

Experimental Design	Pond	River
Duration of the test	361 days	
Water:		
Type and size of filter used	Not reported	
Amount of sediment and water per treatment:		
Water (mL)	500 mL	
Sediment (g)[1]	218-256 (*ca.* 2 cm height)	205-251 (*ca.* 2 cm height)
Water:sediment ratio	*ca.* 2:1	
Application rates:		
Nominal	Not reported	
Actual	0.1349 mg/sample (*ca.* 0.27 mg/L), equivalent to a field rate of 0.9 kg a.i./ha (0.8 lb a.i./A)	
Number of replicates:		
Control, if used	Sterile controls were not used.	
Treated	Single samples (one entire flask) of each test system were collected at each sampling interval.	
Test apparatus:		

Experimental Design	Pond		River	
Type/material/volume	Glass metabolism flasks (1-L; 10-cm i.d.; 78.5 cm^2 surface area) containing water and sediment were attached to flow-through volatile trapping systems and incubated in darkness in a temperature-controlled environmental chamber. The test systems were acclimated for 31 days (pond) or 51 days (river) prior to treatment. The water was gently stirred from the top during incubation. The test apparatus is illustrated in Figure 2, p. 55.			
Details of traps for CO_2 and organic volatile, if any	Humidified air was drawn through a sample (60 mL/minute), then through one bottle of ethylene glycol, one bottle of 0.25N H_2SO_4, and two bottles of 2N NaOH. The volatile trapping system is illustrated in Figure 2, p. 55.			
If no traps were used, is the system closed?	Volatile traps were used.			
Identity and final concentration (based on water volume) of co-solvent	Methanol, 0.01% by volume			
Test material application method:				
Volume of the test solution used/treatment	54 µL/sample			
Application method (*i.e.*, mixed/not mixed)	Applied to the water using a Hamilton syringe			
Any indication of the test material adsorbing to the walls of the test apparatus?	None			
Microbial biomass (as mg C/100 g)	Initial	Final	Initial	Final
Water	Not reported			
Sediment	422	281	243	118
Experimental conditions:				
Temperature	20 ± 2°C, range 18.9-20.9°C			
Continuous darkness (yes/no)	Yes			
Other details (if any)	None			

Data obtained from pp. 22-27, 35; Table 4, p. 46; and Figure 2, p. 55, of the study report.
1 It was not stated if the sediment weights were reported as dry or weight.

2. Sampling during Study Period: **Table 6** summarizes sampling during the study period.

Table 6. Sampling during Study Period

Parameter	Details
Sampling intervals (duration)	0, 7, 14, 28, 60, 120, 203, 280, and 361 days posttreatment.
Sampling method	Single samples (one entire flask) of each test system were collected at each sampling interval.
Method of collection of CO_2 and organic volatile compounds	Volatile traps were collected at each sampling interval, and were exchanged at weekly intervals during the first month and at 2-week intervals thereafter.
Sampling Intervals/Times	
Redox potential in water layer	Measured at each sampling interval
Dissolved oxygen in water layer	
pH in water layer	
Redox potential in sediment	
pH in sediment	
Other details, if any	Water and sediment extracts were separated on the day of sampling. It was not stated if the water and sediment were stored prior to extraction and analysis. Storage of samples when not in use was not described.

Data obtained from p. 25 of the study report.

3. Analytical Procedures:

Separation of the Water and Sediment: The water layer was removed from the sediment (p. 25). A portion of water was concentrated using a rotary evaporator (35°C) and analyzed using HPLC.

Extraction/Clean Up/Concentration Methods: The sediment was extracted up to six times with acetonitrile: water (4:1, v:v) by shaking (30 minutes) at ambient temperatures (pp. 25-28). After each extraction, the samples were centrifuged and the supernatant decanted. The extracts were combined. The sediment was then Soxhlet-extracted with acetonitrile for 8 hours, and the extract and sediment were separated by centrifuging.

Extracted sediment from 203 and 280 days posttreatment was then extracted by refluxing first with acetonitrile:water (4:1, v:v) for 1-2 hours and then with acetonitrile:0.1N HCl (9:1, v:v) for 1-2 hours (p. 26; Table 8, p. 50).

Aliquots of liquid samples (presumed to be water and sediment extracts) were analyzed using LSC (p. 27: Tables 6-7, pp. 48-49).

Determination of Unextracted Residues: The extracted soils were homogenized and analyzed for total remaining radioactivity using LSC following combustion (p. 26).

Determination of Volatile Compounds: Aliquots of the trapping solutions were analyzed by LSC (p. 26). Residues in the trapping solutions were confirmed to be CO_2 by reacting the trapping solution with H_2SO_4.

Total Radioactivity Measurement: Total [^{14}C]residues were determined by summing the concentrations of residues measured in the water layer, sediment extracts, extracted sediment and trapping solutions (Tables 6-7, pp. 48-49).

Derivatization Method: A derivatization method was not described.

Identification and quantification of Parent and Transformation Compounds: Aliquots of the water and sediment extracts were analyzed by HPLC using a Nucleosil C-18 column eluted with a gradient mobile phase of (A) water and (B) acetonitrile with UV and radioactive flow detection (pp. 28-30).

To confirm the results of the HPLC analyses, aliquots of the extracts were analyzed by two-dimensional TLC on silica gel plates developed in ethyl acetate:methanol:water (60:30:5, v:v:v), chloroform:methanol:formic acid:water (75:20:4:2 and 75:20:4:1, v:v:v:v), chlorform:methanol:water (75:20:2 and 60:30:5, v:v:v), and dichlormethane:methanol:ammoninum hydroxide (60:40:2, v:v:v; pp. 31-32). Radioactive regions were located and quantified using autoradiography.

HPLC peaks and TLC regions of radioactivity were identified by comparison to reference standards that were cochromatographed with the samples (pp. 30, 31-32).

The identity of transformation products was confirmed using spectroscopy (not described, pp. 38-39).

Detection Limits (LOD, LOQ) for the Parent and Transformation Products: Limits of Detection (LOD) and Quantification (LOQ) were not reported.

II. Results and Discussion

A. Data:

Study results, including total mass balances and distribution of radioactivity, are presented in **Tables 7a-7b**. In the water columns of the pond systems following treatment, redox potentials and oxygen saturation were +151 to +307 mV and 6.0-7.1 mg/L, respectively, with redox potentials in the sediment of -92 to -34 mV and pHs of the test system of 8.43-8.72 (Table 4, p. 46). In the water columns of the river systems, redox potentials and oxygen saturation were +174 to +313 mV and 6.1-7.3 mg/L, respectively, with redox potentials in the sediment of -81 to -30 mV and pHs of the test systems of 8.44-8.67.

Pond sediment microbial biomass was 422 mg C/100 g at study start and 281 mg C/100 g at study end (p. 35). River sediment microbial biomass was 243 mg C/100 g at study start and 118 mg C/100 g at study end.

B. Mass Balance:

In pond water:silt loam sediment systems, overall recoveries averaged 105.94 ± 2.94% (sample range 100.16-109.51%) of the applied (Table 6, p. 48). Recoveries were within guideline criteria (90-110%). In the water column, pymetrozine decreased from a maximum of 98.10% at time 0 to 0.24-0.33% at 280-361 days posttreatment (Table 10, p. 52). Pymetrozine concentrations in the sediment extracts were not reported.

In river water:silt loam sediment systems, overall recoveries averaged 105.67 ± 3.00% (sample range 100.07-108.59%) of the applied (Table 7, p. 49). Recoveries were within guideline criteria (90-110%). In the water column, pymetrozine decreased from a maximum of 96.74% at time 0 to 0.36% at 361 days posttreatment (Table 11, p. 53). Pymetrozine concentrations in the sediment extracts were not reported.

C. Bound and Extractable Residues:

In the water from the pond water:sediment systems, radioactive residues decreased from 99.39% of the applied at time 0 to 3.98% at 361 days posttreatment (Table 6, p. 48). In the sediment, extractable radioactivity increased from 0.55% at time 0 to a maximum of 57.25% at 28 days and was 32.74% at 361 days. Soxhelt extraction of the sediments released up to an additional 3.41%. Unextracted radioactivity increased from 0.23% at time 0 to a maximum of 46.88% at 203 days and was 43.31% at 361 days. Harsh extraction [refluxing with acetonitrile:water (4:1, v:v) and acetonitrile:0.01M HCl (9:1, v:v)] of the sediment at 203 days released an additional 2.06% (Table 8, p. 50).

In the water from the river water:sediment systems, radioactive residues decreased from 98.82% of the applied at time 0 to 6.74-7.10% at 280-361 days posttreatment (Table 7, p. 49). In the sediment, extractable radioactivity increased from 1.04% at time 0 to a maximum of 62.55% at 28 days and was 31.49% at 361 days. Soxhelt extraction of the sediments released up to an additional 4.67%.

Unextracted radioactivity increased from 0.21% at time 0 to a maximum of 43.27% at 361 days. Harsh extraction of the sediment at 203 days released an additional 2.06% (Table 8, p. 50).

D. Volatilization:

In the pond water:sediment test systems, CO_2 was a maximum of 24.66% of the applied at 361 days posttreatment (Table 6, p. 48). Organic volatile compounds were not detected at any sampling interval.

In the river water:sediment test systems, CO_2 was a maximum of 22.89% of the applied at 361 days posttreatment (Table 7, p. 49). Organic volatile compounds were not detected at any sampling interval.

Table 7a. Aerobic transformation of [triazinyl-6-^{14}C]Pymetrozine, expressed as a percentage of the applied radioactivity, in pond water:silt loam sediment.

Sampling Interval (days)	0	7	14	28	60	120	203	280	361
Replicate Number	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**
Pymetrozine (CGA 215944)	98.10	85.44	66.38	56.09	44.57	40.20	27.33	21.63	27.64
Metabolite D	1.29	6.39	17.72	17.39	10.52	7.05	4.28	3.66	1.94
Unknown A-1	0.00	0.00	0.00	0.51	0.45	0.37	0.51	0.35	1.78
Unknown A-2	0.00	1.44	1.44	1.70	0.73	0.75	0.38	1.61	0.98
Unknown A-3	0.00	0.00	0.00	0.38	0.94	0.00	0.00	0.00	0.72
Unknown B	0.00	0.86	1.17	1.95	3.60	2.02	3.70	1.93	1.21
Unknown C	0.00	0.45	0.00	0.45	0.00	0.50	1.17	1.67	2.45
Water	99.39	41.12	30.04	21.25	13.57	6.89	5.70	4.17	3.98
Extractable residues	0.55	53.47	56.65	57.25	47.24	44.00	31.67	26.70	32.74
Soxhlet extractable	0.00	0.19	0.27	0.41	2.72	3.41	0.68	3.16	0.22
Unextracted residues	0.23	14.70	21.02	26.16	35.98	43.31	46.88	45.52	43.31
CO_2	0.00	0.03	0.23	1.30	5.58	11.86	20.70	24.54	24.66
Volatile organics	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Mass balance	100.16	109.51	108.20	106.38	105.08	109.48	105.62	104.09	104.90

Data obtained from Table 6, p. 48, and Table 10, p. 52, of the study report.
Metabolite D = CGA 359009; 4,5-Dihydro-5-hydroxy-6-methyl-4-[(3-pyridinylmethylene)amino]-1,2,4-triazine-3-(2H)-one.
Metabolite B = CGA 294849; 4-Amino-6-methyl-1,2,4-triazine-3,5(2H,4H)-dione.
Metabolite C = CGA 3710754; 4,6-Dimethyl-2H-1,2,4-triazine-3,5-dione.

Table 7b. Aerobic transformation of [triazinyl-6-^{14}C]Pymetrozine, expressed as a percentage of the applied radioactivity, in river water:silt loam sediment.

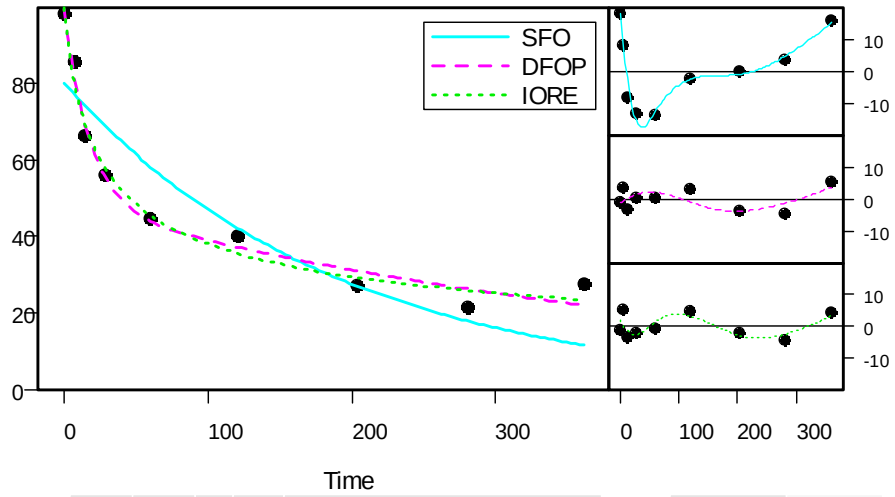
Sampling Interval (days)	0	7	14	28	60	120	203	280	361
Replicate Number	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**
Pymetrozine (CGA 215944)	96.74	91.63	82.86	70.84	56.68	46.06	31.93	36.43	25.08
Metabolite D	0.00	5.11	10.11	12.44	12.02	7.37	4.86	2.76	2.09
Unknown A-1	0.00	0.00	0.00	0.00	0.00	0.29	0.40	0.30	0.40
Unknown A-2	0.00	1.24	0.77	1.45	1.74	0.95	1.40	0.51	2.49
Unknown A-3	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Unknown B	2.08	3.73	0.00	2.04	4.85	2.64	5.87	2.82	3.96
Unknown C	0.00	0.00	0.00	0.70	0.00	0.31	2.75	1.84	4.59
Unknown E	0.00	0.00	0.00	0.00	0.00	0.00	1.16	0.00	0.00
Water	98.82	47.79	38.65	24.94	16.15	8.75	9.66	6.74	7.10
Extractable residues	1.04	53.96	55.09	62.55	59.12	48.86	38.64	37.91	31.49
Soxhlet extractable	0.00	0.15	0.66	0.48	3.21	4.67	1.04	3.56	0.30
Unextracted residues	0.21	6.56	11.70	19.83	27.53	37.45	40.63	36.75	43.27
CO_2	0.00	0.05	0.17	0.66	2.58	6.15	16.45	16.85	22.89
Volatile organics	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Mass balance	100.07	108.51	106.27	108.47	108.59	105.89	106.42	101.80	105.05

Data obtained from Table 7, p. 49, and Table 11, p. 53, of the study report.
Metabolite D = CGA 359009; 4,5-Dihydro-5-hydroxy-6-methyl-4-[(3-pyridinylmethylene)amino]-1,2,4-triazine-3-(2H)-one.
Metabolite B = CGA 294849; 4-Amino-6-methyl-1,2,4-triazine-3,5(2H,4H)-dione.
Metabolite C = CGA 3710754; 4,6-Dimethyl-2H-1,2,4-triazine-3,5-dione.

E. Transformation of Parent Compound: Transformation kinetics of the parent compound in the total system are summarized in the following **Figure**, with transformation product information summarized in **Table 8**. Transformation kinetics for Metabolite D are presented in DER Attachment 2.

Using the MicroCal Origin 3.5, the study author calculated overall total system DT50 values of 40.7 days for the pond system and 93.3 days for the river system (pp. 32-33, 37-38; Table 9, p. 51).

Pymetrozine in aerobic pond water:silt loam sediment

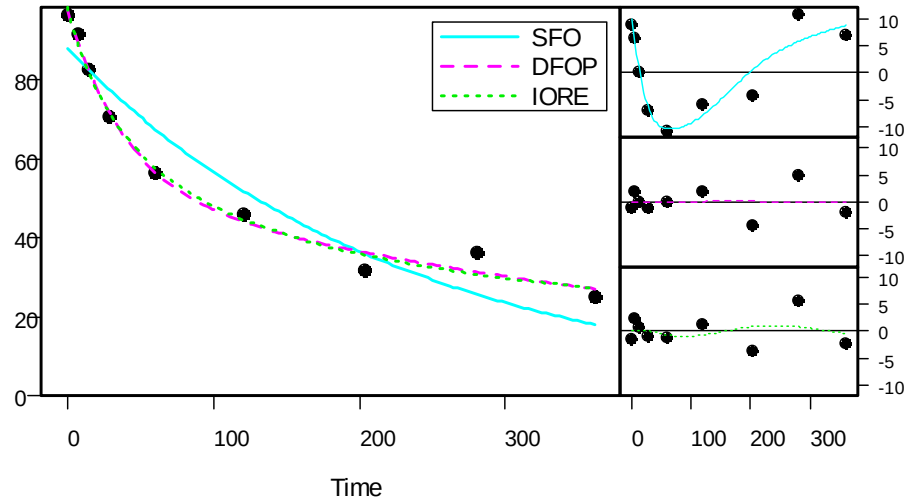


Da	%AR
0	98.1
7	85.4
14	66.4
28	56.1
60	44.6
120	40.2
200	27.3
280	21.6
360	27.6

	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	13	43	1	8	k 0.00532
DFOP	39.	73	5.	99	f 0.514 k_0 0.057 k_1 0.00216
IORE	46.	327	5.	99	N 3.53 k 3.61e-07

S_C	153
S_{SFO}	1.08e+03
Slow $t_{1/2}$	321
$t_{R\ IORE}$	985

Pymetrozine in aerobic river water:silt loam sediment



Da	%AR
0	96.7
7	91.6
14	82.9
28	70.8
60	56.7
120	46.1
200	31.9
280	36.4
360	25.1

	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	15	52	1	87	k 0.00438
DFOP	90.	91	3.	97	f 0.465 k_0 0.0255 k_1 0.00183
IORE	94.	275	3.	98	N 2.91 k 2.4e-06

S_C	92.4
S_{SFO}	500
Slow $t_{1/2}$	379
$t_{R\ IORE}$	828

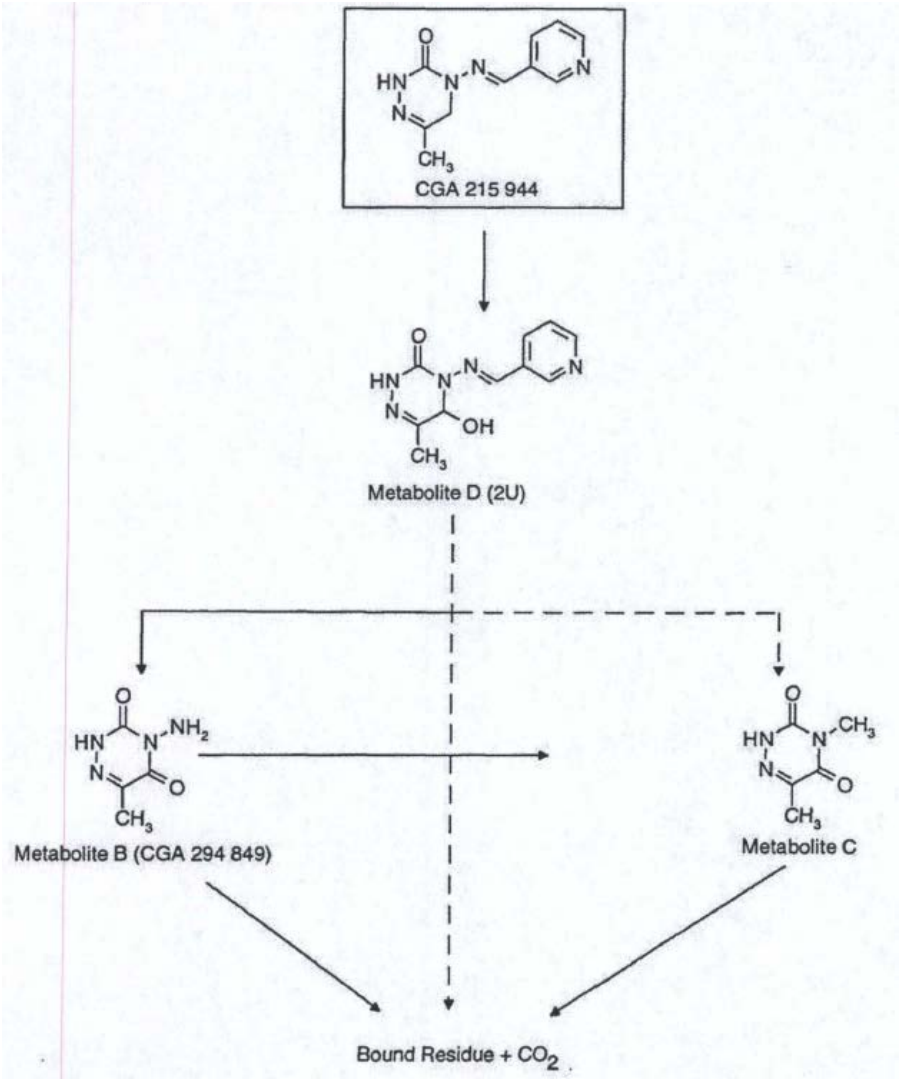
Kinetics models: Single First Order (SFO); Double First Order in Parallel (DFOP), and Indeterminate Order Rate Equation (IORE) in accordance with NAFTA kinetics guidance (USEPA, 2012).

Table 8. Transformation Products of Pymetrozine in the Water:Sediment Systems.

	Transformation Products	Maximum %AR Observed	Associated Interval (days)	Final %AR Observed	Final Interval (days)
Switzerland Pond water:silt loam sediment, (20°C, water pH not reported, sediment pH 6.80)	Metabolite B	3.70	203	1.21	361
	Metabolite C	2.45	361	2.45	361
	Metabolite D	17.72	14	1.94	361
Switzerland Rhine River water:silt loam sediment, (20°C, water pH not reported, sediment pH 7.10)	Metabolite B	5.87	203	3.96	361
	Metabolite C	4.59	361	4.59	361
	Metabolite D	12.44	28	2.09	361

Data obtained from Tables 10-11, pp. 52-53, in the study report.
Metabolite B = CGA 294849; 4-Amino-6-methyl-1,2,4-triazine-3,5(2H,4H)-dione.
Metabolite C = CGA 3710754; 4,6-Dimethyl-2H-1,2,4-triazine-3,5-dione.
Metabolite D = CGA 359009; 4,5-Dihydro-5-hydroxy-6-methyl-4-[(3-pyridinylmethylene)amino]-1,2,4-triazine-3-(2H)-one.

A transformation pathway was provided by the study author (Figure 28, p. 81).



III. Study Deficiencies and Reviewer's Comments

1. Significant levels (43.27-46.88% of the applied) of unextracted residues were detected (Tables 6-7, pp. 48-49). The study author failed to use solvents with a range of dielectric constants (including a nonpolar solvent) to maximize extraction of the residues. However, two subsequent extraction steps were performed, and extracts did not exceed 2.06% if the applied radioactivity, so the material was not further analyzed.

2. Both test systems consisted of silt loam sediment with an organic carbon contents of 3.2-3.7%, and had pHs that were alkaline (*ca*. pH 8.5) during the experiments (Table 2, p. 44; Table 4, p. 46).

3. It was not stated if the sediment was stored prior to extraction. Length and conditions of storage of the water and sediment extract prior to analysis were not reported. Storage of samples when not in use was not described.

4. Limits of Detection (LOD) and Quantification (LOQ) were not reported.

5. The pesticide use history at the source sites was not reported, and it was not demonstrated that the water and sediment were free of pesticides prior to use.

6. It was unclear how long the samples were preincubated before treatment. Pre-incubation is reported to be 21 days for both systems on p. 16, but 31 days for the pond system and 51 days for the river system on p. 23.

7. The recommended field rate was reported to be 0.3 kg a.i./ha (p. 16). The treatment rate used in the study was 0.9 kg a.i./ha.

8. The study author describes Application Solution 2, which was used to treat samples that were immediately analyzed (pp. 24, 34). It was not stated if these were time 0 samples or served some other purpose.

9. Four reference compounds expired before the completion of the study.

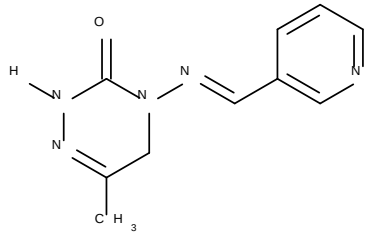
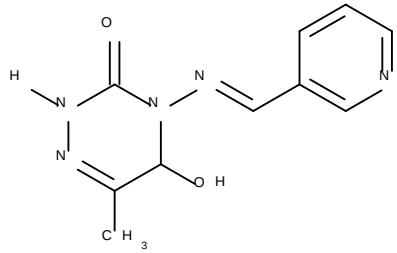
10. In other aerobic aquatic metabolism studies, the half-life observed from both radiolabels in MRID 49921304 was much faster than the half-lives calculated in this study. MRID 49921306 involved the pyridine moiety, and had longer, but comparable pymetrozine half-lives to that of this study.

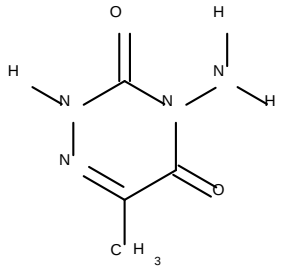
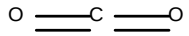
IV. References

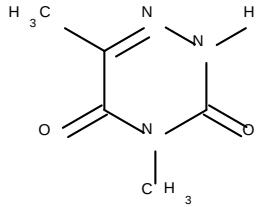
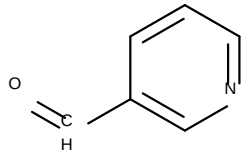
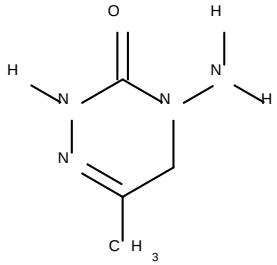
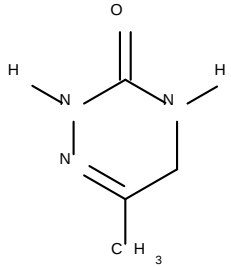
1. U.S. Environmental Protection Agency. 2008. Fate, Transport and Transformation Test - Guidelines, OPPTS 835.4300, Aerobic Aquatic Metabolism. Office of Prevention, Pesticides and Toxic Substances, Washington, DC. EPA 712-C-08-018.

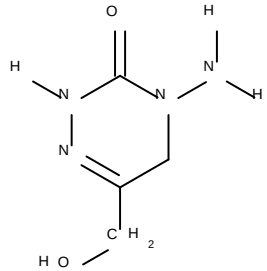
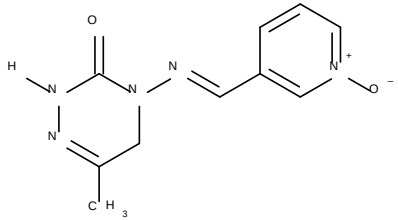
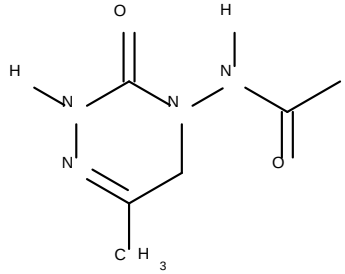
2. U.S. Environmental Protection Agency. 2012. NAFTA Guidance for Evaluating and Calculating Degradation Kinetics in Environmental Media.

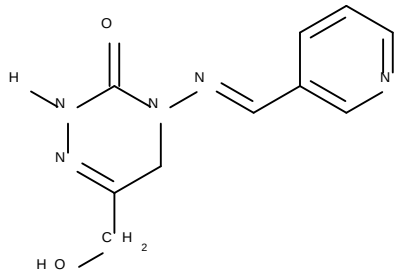
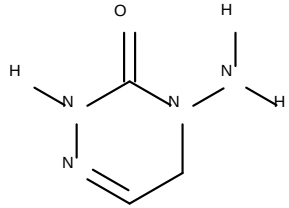
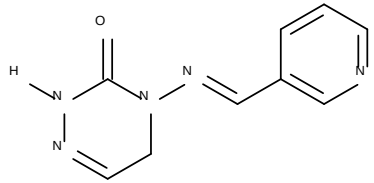
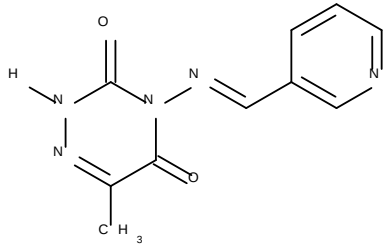
DER ATTACHMENT 1. Pymetrozine and Its Environmental Transformation Products. [A]

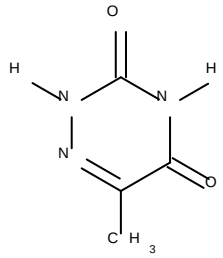
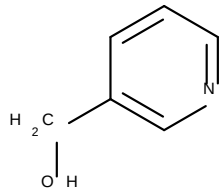
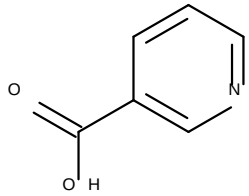
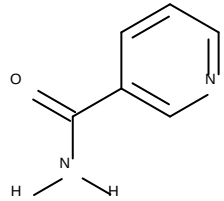
Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)		Final %AR (study length)
PARENT							
Pymetrozine (CGA 215944, CSAA202913)	**IUPAC:** (E)-4,5-dihydro-6-methyl-4-(3-pyridylmethyleneamino)-1,2,4-triazin-3(2H)-one **CAS:** 4,5-dihydro-6-methyl-4-[(E)-(3-pyridinylmethylene)amino]-1,2,4-triazin-3(2H)-one **CAS No.:** 123312-89-0 **Formula:** $C_{10}H_{11}N_5O$ **MW:** 217.2 g/mol **SMILES:** O=C1NN=C(C)CN1N=Cc2cccnc2		835.4300 Aerobic aquatic metabolism	49921304 49921305 49921306	PRT		PRT
MAJOR (>10%) TRANSFORMATION PRODUCTS							
CGA 359009 (CSAA441607, Metabolite D, M4, Metabolite 2U)	**IUPAC:** 4,5-Dihydro-5-hydroxy-6-methyl-4-[(3-pyridinylmethylene)amino]-1,2,4-triazine-3-(2H)-one **Formula:** $C_{10}H_{11}N_5O_2$ **MW:** 233.2 g/mol **SMILES:** CC1=NNC(=O)N(\N=C\c2cccnc2)C1O		835.4300 Aerobic aquatic metabolism	49921304	River waer:sand	**12.4%** (7 d)	1.1% (102 d)
				49921305	Pond water:silt loam	**17.72%** (14 d)	1.94% (361 d)
					River water:silt loam	**12.44%** (28 d)	2.09% (361 d)
				49921306	Pond water:silt loam	**10.77%** (28 d)	2.21% (344 d)
					River water:silt loam	**10.88%** (60 d)	2.48% (344 d)

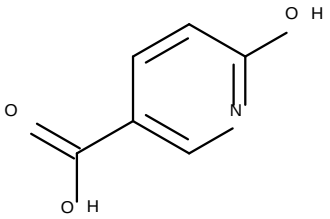
Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)		Final %AR (study length)
CGA 294849 (CSAA377032, Metabolite B)	**IUPAC:** 4-Amino-6-methyl-1,2,4-triazine-3,5(2H,4H)-dione **Formula:** $C_4H_6N_4O_2$ **MW:** 142.1 g/mol **SMILES:** CC1=NNC(=O)N(N)C1=O		835.4300 Aerobic aquatic metabolism	49921304	River waer:sand	**9.8%** (14 d)	1.4% (102 d)
				49921305	Pond water:silt loam	3.70% (203 d)	1.21% (361 d)
					River water:silt loam	5.87% (203 d)	3.96% (361 d)
Carbon dioxide	**IUPAC:** Carbon dioxide **Formula:** CO_2 **MW:** 44 g/mol **SMILES:** C(=O)=O		835.4300 Aerobic aquatic metabolism	49921304	River waer:sand	**54.1%** (102 d)	**54.1%** (102 d)
				49921305	Pond water:silt loam	**24.66%** (361 d)	**24.66%** (361 d)
					River water:silt loam	**22.89%** (361 d)	**22.89%** (361 d)
				49921306	Pond water:silt loam	**36.30%** (285 d)	**28.56%** (344 d)
					River water:silt loam	**33.78%** (285 d)	**32.12%** (344 d)
Unextractable residues	NA	NA	835.4300 Aerobic aquatic metabolism	49921304	River waer:sand	**60.6%** (61 d)	**53.3%** (102 d)
				49921305	Pond water:silt loam	**46.88%** (203 d)	**43.31%** (361 d)
					River water:silt loam	**43.27%** (361 d)	**43.27%** (361 d)
				49921306	Pond water:silt loam	**22.66%** (285 d)	**21.18%** (344 d)
					River water:silt loam	**23.21%** (344 d)	**23.21%** (344 d)

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)		Final %AR (study length)
MINOR (<10%) TRANSFORMATION PRODUCTS							
CGA 371075 (CSAA447511, Metabolite C)	**IUPAC:** 4,6-Dimethyl-2H-1,2,4-triazine-3,5-dione **Formula:** $C_5H_7N_3O_2$ **MW:** 141.1 g/mol **SMILES:** CN1C(=O)NN=C(C)C1=O		835.4300 Aerobic aquatic metabolism	49921305	Pond water:silt loam	2.45% (361 d)	2.45% (361 d)
					River water:silt loam	4.59% (361 d)	4.59% (361 d)
CGA 300407 (M3)	**IUPAC:** 3-pyridinecarboxaldehyde **Formula:** C_6H_5NO **MW:** 107.1 g/mol **SMILES:** O=Cc1cccnc1		835.4300 Aerobic aquatic metabolism	49921306	Pond water:silt loam	2.93% (120 d)	2.05% (344 d)
					River water:silt loam	4.47% (210 d)	2.17% (344 d)
REFERENCE COMPOUNDS NOT IDENTIFIED							
CGA 215525	**IUPAC:** 4-Amino-6-methyl-2,5-dihydro-1,2,4-triazin-3-one **Formula:** $C_4H_8N_4O$ **MW:** 128.1 g/mol **SMILES:** CC1=NNC(=O)N(N)C1		835.4300 Aerobic aquatic metabolism	49921305	NA		NA
CGA 249257	**IUPAC:** 6-Methyl-4,5-dihydro-2H-1,2,4-triazin-3-one **Formula:** $C_4H_7N_3O$ **MW:** 113.1 g/mol **SMILES:** CC1=NNC(=O)NC1		835.4300 Aerobic aquatic metabolism	49921305	NA		NA

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (study length)
CGA 311892	**IUPAC:** 4-Amino-6-(hydroxymethyl)-2,5-dihydro-1,2,4-triazin-3-one **Formula:** $C_4H_8N_4O_2$ **MW:** 144.1 g/mol **SMILES:** NN1CC(=NNC1=O)CO		835.4300 Aerobic aquatic metabolism	49921305	NA	NA
CGA 245342	**IUPAC:** 6-Methyl-4-[(E)-(1-oxidopyridin-1-ium-3-yl)methyleneamino]-2,5-dihydro-1,2,4-triazin-3-one **Formula:** $C_{10}H_{11}N_5O_2$ **MW:** 233.2 g/mol **SMILES:** CC1=NNC(=O)N(C1)\N=C\c2ccc[n+]([O-])c2		835.4300 Aerobic aquatic metabolism	49921305	NA	NA
CGA 259168	**IUPAC:** N-(6-methyl-3-oxo-2,5-dihydro-1,2,4-triazin-4-yl)acetamide **Formula:** $C_6H_{10}N_4O_2$ **MW:** 170.2 g/mol **SMILES:** CC(=O)NN1CC(=NNC1=O)C		835.4300 Aerobic aquatic metabolism	49921305	NA	NA

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (study length)
CGA 313124	**IUPAC:** 6-(Hydroxymethyl)-4-[(E)-3-pyridylmethyleneamino]-2,5-dihydro-1,2,4-triazin-3-one **Formula:** $C_{10}H_{11}N_5O_2$ **MW:** 233.2 g/mol **SMILES:** OCC1=NNC(=O)N(C1)\N=C\c2cccnc2		835.4300 Aerobic aquatic metabolism	49921305 49921306	NA	NA
CGA 320481	**IUPAC:** 4-Amino-2,5-dihydro-1,2,4-triazin-3-one **Formula:** $C_3H_6N_4O$ **MW:** 114.1 g/mol **SMILES:** NN1CC=NNC1=O		835.4300 Aerobic aquatic metabolism	49921305	NA	NA
CGA 320484	**IUPAC:** 4-[(E)-3-pyridylmethyleneamino]-2,5-dihydro-1,2,4-triazin-3-one **Formula:** $C_9H_9N_5O$ **MW:** 203.2 g/mol **SMILES:** O=C1NN=CCN1\N=C\c2cccnc2		835.4300 Aerobic aquatic metabolism	49921305 49921306	NA	NA
CGA 323584	**IUPAC:** 6-Methyl-4-[(E)-3-pyridylmethyleneamino]-2H-1,2,4-triazine-3,5-dione **Formula:** $C_{10}H_9N_5O_2$ **MW:** 231.2 g/mol **SMILES:** CC1=NNC(=O)N(\N=C\c2cccnc2)C1=O		835.4300 Aerobic aquatic metabolism	49921305 49921306	NA	NA

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (study length)
GS 23199	**IUPAC:** 6-Methyl-2H-1,2,4-triazine-3,5-dione **Formula:** $C_4H_5N_3O_2$ **MW:** 127.1 g/mol **SMILES:** CC1=NNC(=O)NC1=O		835.4300 Aerobic aquatic metabolism	49921305	NA	NA
CGA 128632	**IUPAC:** 3-Pyridylmethanol **Formula:** C_6H_7NO **MW:** 109.1 g/mol **SMILES:** OCc1cccnc1		835.4300 Aerobic aquatic metabolism	49921306	NA	NA
CGA 180777	**IUPAC:** Nicotinic acid **Formula:** $C_6H_5NO_2$ **MW:** 123.1 g/mol **SMILES:** OC(=O)c1cccnc1		835.4300 Aerobic aquatic metabolism	49921306	NA	NA
CGA 180778	**IUPAC:** Pyridine-3-carboxamide **Formula:** $C_6H_6N_2O$ **MW:** 122.1 g/mol **SMILES:** NC(=O)c1cccnc1		835.4300 Aerobic aquatic metabolism	49921306	NA	NA

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (study length)
CGA 319251	**IUPAC:** 6-Hydroxypyridine-3-carboxylic acid **Formula:** $C_6H_5NO_3$ **MW:** 139.1 g/mol **SMILES:** OC(=O)c1ccc(O)nc1		835.4300 Aerobic aquatic metabolism	49921306	NA	NA

[A] AR means “applied radioactivity”. MW means “molecular weight”. PRT means “parent”. NA means “not applicable”.

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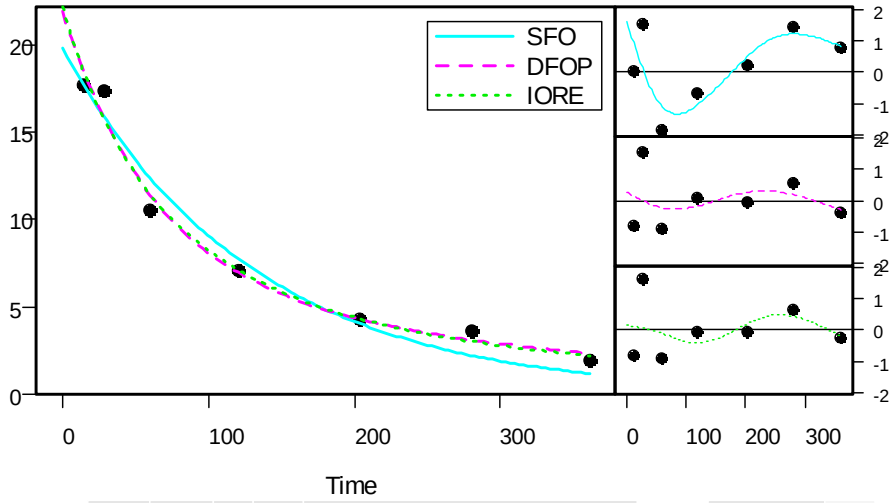
Attachment 2: Statistics Spreadsheets and Graphs

Metabolite D in aerobic pond water:silt loam sediment

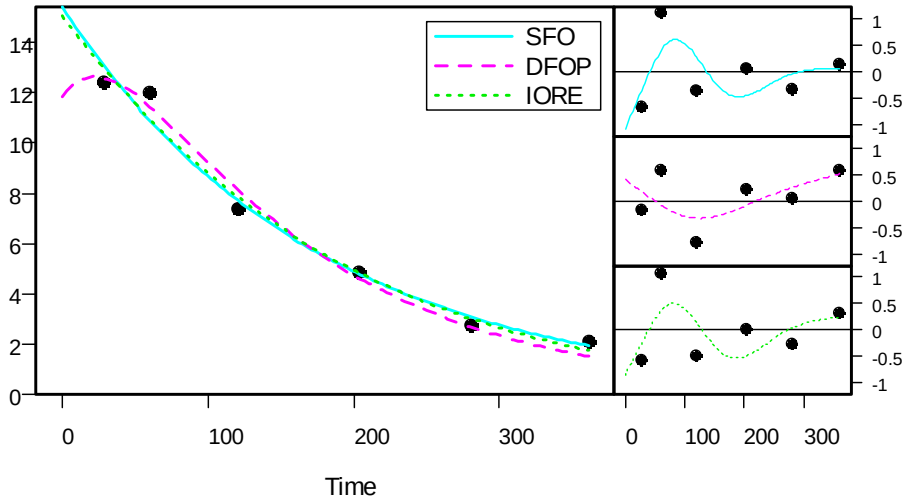


Da	%AR
1	17.7
2	17.4
6	10.5
12	7.05
20	4.28
28	3.66
36	1.94

	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	8	29	1	19	k 0.00779
DFO	64.	38	8.	21	f 0.666 k_0 0.0166 k_1 0.00319
IOR	6	36	7.	22	N 1.58 k 0.00221

S_C	7.9
S_{SFO}	8.88
Slow $t_{1/2}$	217
$t_{R\ IORE}$	109

Metabolite D in aerobic river water:silt loam sediment



Da	%AR
2	12.4
6	12.0
12	7.37
20	4.86
28	2.76
36	2.09

	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	12	40	6.	15	k 0.00573
DFO	16	39	6.	11	f -0.673 k_0 0.0282 k_1 0.00711
IOR	12	38	7.	15	N 0.875 k 0.00731

S_C	3.72
S_{SFO}	1.94
Slow $t_{1/2}$	97.5
$t_{R\ IORE}$	116

Kinetics models: Single First Order (SFO); Double First Order in Parallel (DFOP), and Indeterminate Order Rate Equation (IORE) in accordance with NAFTA kinetics guidance (USEPA, 2012).

Attachment 3: Calculations

Calculations were performed by the reviewer using R software, and the following equations.

Single First-Order (SFO) Model

$$C_t = C_0 e^{-kt} \quad \text{(eq. 1)}$$

where,

C_t = concentration at time t (%)
C_0 = initial concentration (%)
e = Euler's number (-)
k = SFO rate constant of decline (d^{-1})
t = time (d)

The SFO equation is solved with R kinetics software by adjusting C_0 and k to minimize the objective function (S_{SFO}) shown in equation 9.

DT_{50} = natural log (2)/k (eq. 2)

DT_{90} = ln (10)/k (eq. 3)

Indeterminate Order Rate Equation (IORE) Model

$$C_t = \left[C_0^{(1-N)} - (1-N)k_{IORE}t\right]^{\left(\frac{1}{1-N}\right)} \quad \text{(eq. 4)}$$

where,

N = order of decline rate (-)
k_{IORE} = IORE rate constant of decline (d^{-1})

This equation is solved with R kinetics software by adjusting C0, kIORE, and N to minimize the objective function for IORE (SIORE) (See equation 9). Half-lives for the IORE model are calculated using equation 5, which represents a first-order half-life that passes through the DT_{90} of the IORE model. (Traditional DT_{50} and DT_{90} values for the IORE model can be calculated using equations 6 and 7.)

$$t_{IORE} = \frac{\log(2)}{\log(10)} \frac{{C_0}^{1-N}\left(1-0.1^{(1-N)}\right)}{(1-N)k_{IORE}} \quad \text{(eq. 5)}$$

$$DT_{50} = \frac{(C_0/2)^{(1-N)} - C_0^{(1-N)}}{k(N-1)} \quad \text{(eq. 6)}$$

$$DT_{90} = \frac{(C_0/10)^{(1-N)} - C_0^{(1-N)}}{k(N-1)} \quad \text{(eq. 7)}$$

Double First-Order in Parallel (DFOP) Model

$$C_t = C_0 g^{-k_1 t} + C_0(1-g)^{-k_1 t} \quad \text{(eq. 8)}$$

where,

g = the fraction of C_0 applied to compartment 1 (-)
k_1 = rate constant for compartment 1 (d^{-1})
k_2 = rate constant for compartment 2 (d^{-1})

If $C_0 \times g$ is set equal to *a* and $C_0(1-g)$ is set equal to *c*, then the equation can be solved with R kinetics software for *a*, *c*, k_1, and k_2 by minimizing the objective function (S_{DFOP}) as described in equation 9.

DT_{50} and DT_{90} values can be calculated using equations 2 and 3, with k_1 or k_2 in place of k.

Objective Function: SFO, IORE, and DFOP are solved by minimizing the objective function (S_{SFO}, S_{IORE}, or S_{DFOP}).

$$S_{SFO}, S_{IORE}, \text{ or } S_{DFOP} = \sum (C_{model,t} - C_{d,t})^2 \quad \text{(eq. 9)}$$

where,

S_{SFO} , S_{IORE}, or S_{DFOP} = objective function of kinetics model fit ($\%^2$)
n = number of data points (-)
$C_{model,t}$ = modeled value at time corresponding to $C_{d,t}$ (%)
$C_{d,t}$ = experimental concentration at time t (%)

Critical Value to Determine Whether SFO is an Adequate Kinetics Model

If S_{SFO} is less than S_C, the SFO model is adequate to describe kinetics. If not, the faster of t_{IORE} or the DFOP DT_{50} for compartment 2 should be used.

$$S_c = S_{IORE}\left(1 + \frac{p}{n-p} F(\alpha, p, n-p)\right) \quad \text{(eq. 10)}$$

where,

S_c = the critical value that defines the confidence contours ($\%^2$)
p = number of parameters (3 in this case)
α = the confidence level (0.50 in this case)
F(α, p, n-p) = F distribution with α level of confidence and degrees of freedom p and n-p